

RECEIVED
CENTRAL FAX CENTER
MAR 02 2007

AMENDMENT TO THE CLAIMS

The Listing of the claims below replace all previous listings.

1. (Previously presented) A method for detecting a for the presence or absence of one or more target nucleic acid sequences in a sample, wherein the sample comprises nucleic acid molecules of higher biological complexity relative to amplified nucleic acid molecules and wherein the sample comprises a wild-type target nucleic acid sequence, one or more mutant target nucleic acid sequences which differ from a wild-type target nucleic acid sequence by at least one nucleotide, or both, the method comprising the steps of:

- a) providing an addressable substrate having wild-type capture oligonucleotides bound thereto, wherein the wild-type capture oligonucleotides have a sequence that is complementary to at least part of a first portion of the wild-type target nucleic acid sequence and one or more different mutant capture oligonucleotides, wherein each mutant capture oligonucleotide has a sequence that is complementary to at least part of the first portion of a specific mutant target nucleic acid sequence;
- b) providing a detection probe comprising detector oligonucleotides, wherein the detector oligonucleotides have a sequence that is complementary to at least part of a second portion of the target nucleic acid sequence of step (a);
- c) contacting the sample with the substrate and the detection probe under conditions that are effective for the hybridization of the capture oligonucleotides to the first portion of the target nucleic acid sequence and the hybridization of the detection probe to the second portion of the target nucleic acid sequence and to allow for discrimination between the wild-type target nucleic acid and said one or more mutant target nucleic acid sequences that differ by at least one nucleotide; and
- d) detecting whether the capture oligonucleotide and detection probe hybridized with the

first and second portions of the target nucleic acid sequence.

2. (Original) The method of claim 1, wherein the target nucleic acid sequence comprises a Single Nucleotide Polymorphism.
3. (Original) The method of claim 1, wherein the single nucleotide difference is recognized by the capture oligonucleotide bound to the substrate.
4. (Original) The method of claim 1, wherein the single nucleotide difference is recognized by the detector oligonucleotides.
5. (Original) The method of claim 1, wherein the target nucleic acid molecules comprise genomic DNA, genomic RNA, expressed RNA, plasmid DNA, mitochondrial or other cell organelle DNA, free cellular DNA, viral DNA or viral RNA, or a mixture of two or more of the above.
6. (Original) The method of claim 1, wherein the substrate comprises a plurality of capture oligonucleotides, each of which can recognize a different single nucleotide polymorphism.
7. (Original) The method of claim 1, wherein the sample comprises more than one nucleic acid target, each of which comprises one or more different single nucleotide polymorphisms.
8. (Original) The method of claim 1, wherein one or more types of detector probes are provided, each of which has detector oligonucleotides bound thereto that are capable of hybridizing with a different nucleic acid target.
9. (Original) The method of claim 1, wherein sample is contacted with the detector probe so that a nucleic acid target present in the sample hybridizes with the detector oligonucleotides on the detector probe, and the nucleic acid target bound to the detector probe is then contacted with the substrate so that the nucleic acid target hybridizes with the capture oligonucleotide on the substrate.

10. (Original) The method of claim 1, wherein sample is contacted with the substrate so that a nucleic acid target present in the sample hybridizes with a capture oligonucleotide, and the nucleic acid target bound to the capture oligonucleotide is then contacted with the detector probe so that the nucleic acid target hybridizes with the detector oligonucleotides on the detector probe.

11. (Original) The method of claim 1, wherein the sample is contacted simultaneously with the detector probe and the substrate.

12. (Original) The method of claim 1, wherein the detector oligonucleotides comprise a detectable label.

13. (Original) The method of claim 12, wherein the detection label allows detection by photonic, electronic, acoustic, opto-acoustic, gravity, electro-chemical, electro-optic, mass-spectrometric, enzymatic, chemical, biochemical, or physical means.

14. (Original) The method of claim 12, wherein the label is fluorescent.

15. (Original) The method of claim 12, wherein the label is luminescent.

16. (Original) The method of claim 12, wherein the label is phosphorescent.

17. (Original) The method of claim 12, wherein the label is radioactive.

18. (Original) The method of claim 12, wherein the label is a nanoparticle.

19. (Original) The method of claim 12, wherein the label is a dendrimer.

20. (Original) The method of claim 12, wherein the label is a molecular aggregate.

21. (Original) The method of claim 12, wherein the label is a quantum dot.

22. (Original) The method of claim 12, wherein the label is a bead.

23. (Original) The method of claim 1, wherein the detector probe is a nanoparticle probe having detector oligonucleotides bound thereto.

24. (Original) The method of claim 23, wherein the nanoparticles are made of a noble metal.

25. (Original) The method of claim 24, wherein the nanoparticles are made of gold or silver.
26. (Original) The method of claim 25, wherein the nanoparticles are made of gold.
27. (Original) The method of claim 23, wherein the detecting comprises contacting the substrate with silver stain.
28. (Original) The method of claim 23, wherein the detecting comprises detecting light scattered by the nanoparticle.
29. (Original) The method of claim 23, wherein the detecting comprises observation with an optical scanner.
30. (Original) The method of claim 23, wherein the detecting comprises observation with a flatbed scanner.
31. (Original) The method of claim 29 or 30, wherein the scanner is linked to a computer loaded with software capable of calculating grayscale measurements, and the grayscale measurements are calculated to provide a quantitative measure of the amount of nucleic acid detected.
32. (Original) The method of claim 23, wherein the oligonucleotides attached to the substrate are located between two electrodes, the nanoparticles are made of a material that is a conductor of electricity, and step (d) comprises detecting a change in conductivity.
33. (Original) The method of claim 32, wherein the electrodes are made of gold and the nanoparticles are made of gold.
34. (Original) The method of claim 32, wherein the substrate is contacted with silver stain to produce the change in conductivity.
35. (Original) The method of claims 23, wherein a plurality of oligonucleotides, each of which can recognize a different target nucleic acid sequence, are attached to the substrate in an array of spots and each spot of oligonucleotides is located between two electrodes, the

nanoparticles are made of a material that is a conductor of electricity, and step (d) comprises detecting a change in conductivity.

36. (Original) The method of claim 35, wherein the electrodes are made of gold and the nanoparticles are made of gold.

37. (Original) The method of claim 35, wherein the substrate is contacted with silver stain to produce the change in conductivity.

38. to 157. (Cancelled)

158. (Currently amended) The method of claim 1 or 38, wherein the target nucleic acid sequence is a portion of the *mecA* gene.

159. to 162. (Cancelled)

163. (Amended) The method of claim 38 1, wherein at least one of the target nucleic acid sequences is a portion of a gene of a *Staphylococcus* bacterium and at least one of the target nucleic acid sequences is a portion of the *mecA* gene.

164. (Amended) The method of claim 38 1, wherein the method is used to distinguish between two or more species of a common genus.

165. (Original) The method of claim 164, wherein the species differ by two or more non-consecutive nucleotides.

166. (Original) The method of claim 164, wherein the species differ by two or more consecutive nucleotides.

167. (Original) The method of claim 164, wherein the species differ by at least one nucleotide.